

Correspondence

Effect on incubating syphilis of penicillin treatment for gonorrhoea

TO THE EDITOR *British Journal of Venereal Diseases*

SIR—In the early days of penicillin therapy for gonorrhoea, many venereologists were concerned about the possibility of masking incubating syphilis. To-day, however, with the much larger dosages currently used, the general feeling seems to be that penicillin therapy for gonorrhoea is more likely to cure incubating syphilis than to mask it. The case here reported, therefore, may give some food for thought.

Case history

A 17-year-old West Indian youth attended the clinic at the Royal Northern Hospital on June 15, 1972, complaining of a urethral discharge of 4 days' duration. He had had intercourse 8 days previously with a casual female contact. Gonorrhoea was diagnosed from a Gram-stained film, and routine treatment, consisting of 1.2 m.u. procaine penicillin intramuscularly, was given.

There was no clinical evidence of syphilis at this time, and a routine VDRL test performed on a blood sample obtained at this visit gave negative results.

The patient had attended the clinic on one previous occasion (March, 1970), when gonorrhoea had been diagnosed; serological tests had been negative at that time.

He returned for routine follow-up on June 19, 1972—a mere 4 days after receiving his penicillin. A small ulcer was now present on the frenum of the penis; it was about 3 mm. in diameter and not indurated. The inguinal lymph nodes were enlarged. Darkground examination of serum from the ulcer revealed numerous motile *Treponema pallidum*.

A further blood specimen was sent to the Venereal Diseases Reference Laboratory; all the tests performed (RPCF, VDRL slide, cardiolipin Wassermann reaction, and FTA-ABS) gave negative results.

A full course of antisyphilitic treatment (1.2 m.u. procaine penicillin daily for 10 days) was given and the chancre healed normally; no Herxheimer reaction occurred.

A female contact of the patient (not the one from whom he had presumably acquired gonorrhoea) attended on June 29, 1972. The patient had had intercourse with her on the previous two nights (while still receiving antisyphilitic treatment); no evidence of either gonorrhoea or syphilis could be found in her case.

Discussion

This case raises a number of interesting issues. On the basis of an analysis of nearly 3,000 cases, Woodcock (1971) concluded that 'penicillin given for gonorrhoea is more

likely to cure incubating syphilis than to mask it'. The present case shows that a dose of 1.2 m.u. procaine penicillin cannot be relied upon to abort incubating syphilis in all circumstances.

This finding is perhaps not wholly unexpected. Schroeter, Turner, Lucas, and Brown (1971), reviewing studies carried out by the US Public Health Service before 1967 to determine the minimum dose of penicillin required to abort incubating syphilis in a single dose, recorded that one case of syphilis developed among 225 syphilis contacts who were followed up after receiving 1.2 m.u. procaine penicillin with aluminium monostearate. However, their own trial indicated that 2.4 m.u. aqueous procaine penicillin gave 100 per cent. protection to 51 patients over a 90-day follow-up period, whereas among 57 placebo-treated controls the infection rate was 30 per cent.; they concluded that 'aqueous penicillin G procaine in doses of 2.4 or 4.8 m.u. is effective therapy for incubating syphilis'.

The present case might be regarded as compatible with this claim, since the dosage used was only half that recommended by Schroeter and others. However, Cornelius, Schroeter, Lester, and Martin (1971) found approximately 8-fold variations in blood levels in patients receiving 2.4 m.u. aqueous procaine penicillin. Moreover, 90 days is not a long follow-up period for syphilis, as Schroeter and others acknowledge, and the possibility that the larger dosage prolonged the incubation period in some cases without eliminating all the treponemes cannot be wholly excluded.

Willcox (1962) held that the concentration of penicillin achieved in the blood is less important than the duration of the penicillinaemia. He believed that even small doses of penicillin aluminium monostearate would completely abort incubating syphilis, but pointed out that the various preparations varied in efficacy—a fact which may help to explain the occurrence of syphilis after 1.2 m.u. procaine penicillin with aluminium monostearate reported by Schroeter and others (1971).

The failure of aqueous procaine penicillin to abort syphilis in the present instance must presumably be attributed to the relatively short period of penicillinaemia. Nevertheless, the rapidity with which the chancre developed and the fact that the lesion was darkground-positive are surprising. Magnuson and Eagle (1945) reviewed nine cases in which syphilis developed after penicillin had been given for gonorrhoea in doses of 80,000 to 100,000 units. In six of these a genital lesion,

in retrospect judged to be syphilitic, was unnoticed until treatment for gonorrhoea had been given; all six lesions were darkground-negative and healed within the following 5 to 15 days. The remaining three patients developed lesions 26 to 33 days after treatment; two of these lesions were darkground-positive.

Magnuson and Eagle also investigated the effect of small doses of penicillin on incubating syphilis in rabbits. In less than $\frac{1}{2}$ of the amount necessary to cure an established infection, penicillin either aborted the infection entirely or significantly prolonged the incubation period. In general, the smaller the inoculum and the earlier penicillin was given, the more likely was it that the infection would be aborted; the suppressive effect was greatest when penicillin was given before the seventh day. It is important to notice that many of the lesions were very small and consisted merely of papules which could easily have been missed had they occurred in a human subject.

It is worth reiterating that, in the case reported here, the lesion was in fact very small and had not been noticed by the patient. It is perhaps reassuring that a frank chancre, containing motile treponemes, did develop. However, the case does demonstrate that routine penicillin treatment of gonorrhoea cannot be regarded as wholly adequate insurance against coincidental syphilis, and this is disturbing. Magnuson and Eagle recommended a

minimum of 4 months' follow-up of gonorrhoea, but experience in clinics to-day suggests that few patients are likely to complete such a long period of surveillance. Moreover, those who fail to attend for follow-up are precisely those who may be expected to be most at risk through promiscuity and carelessness about their health; by the same token, they would also constitute a reservoir of potential infection.

This case strengthens the argument for separate reporting of dual infections, first proposed by Leeming as long ago as 1947 and endorsed by Woodcock (1971).

Yours faithfully,

ANTHONY CAMPBELL

ST. MARY'S HOSPITAL,
PRAED STREET,
LONDON, W.1.
March 3, 1974

References

- CORNELIUS, C. E., III, SCHROETER, A. L., LESTER, A., and MARTIN, J. E., Jr. (1971) *Brit. J. vener. Dis.*, **47**, 359
LEEMING, J. A. L. (1947) *Ibid.*, **23**, 155
MAGNUSON, H. J., and EAGLE, H. (1945) *Amer. J. Syph.*, **29**, 587
SCHROETER, A. L., TURNER, R. H., LUCAS, J. B., and BROWN, W. J. (1971) *J. Amer. med. Ass.*, **218**, 711
WILLCOX, R. R. (1962) *Brit. J. vener. Dis.*, **38**, 109
WOODCOCK, K. R. (1971) *Ibid.*, **47**, 95

Ultrastructure of *T. vaginalis*

TO THE EDITOR *British Journal of Venereal Diseases*

SIR—The paper by Ovčinnikov, Delektorskij, and Kosmacheva (1974) requires some comment in the light of recent advances in the study of the ultrastructure and biochemistry of *Trichomonas vaginalis* and other trichomonad species, including the urogenital parasite of cattle *Trichomonas foetus*.

My work in this laboratory on the ultrastructure of *T. vaginalis* confirms that reported by Nielsen, Ludvik, and Nielsen (1966) with regard to the association of the flagellar apparatus and the axostyle. The axostyle is a single sheet of microtubules running parallel to the longitudinal axis of the cell. The sheet is coiled like a cone at the posterior end where it projects from the cell for a distance of several microns; at the anterior end of the cell the sheet flattens out and terminates at the side of the kinetosomes of the five flagella. Lying next to, but apparently not attached to, the anterior end of the axostyle is a smaller sheet of microtubules running at right-angles to the axostyle and curving around the kinetosomes; this is known as the pelta. The organelle identified by Ovčinnikov and others (1974) as the 'parabasal apparatus'

is, I believe, the anterior end of the axostyle and the pelta and not, as they suggest, a separate structure.

The identification as lysosomes of the numerous electron dense granules with their single membrane and granular matrix, a characteristic component of the cytoplasm of trichomonads, lacks corroboration by other workers. Lysosomes have the common property of containing acid hydrolases encompassed in a semi-permeable limiting membrane. Their role in the cell is thought to involve the intracellular digestion of both endogenous and exogenous material (Cohn and Fedorko, 1969). Müller (1973) investigated the enzyme content of the different subcellular components of *T. foetus* and found that the electron dense granules contained no acid phosphatase, an enzyme marker of lysosomes, but that the enzyme was found in a larger population of granules more heterogeneous in size with pleomorphic contents, probably phagocytosed material. Subsequently, Lindmark and Müller (1973) named the electron dense granules of *T. foetus* as hydrogenosomes due to their involvement in the anaerobic trichomonads in the production of hydrogen. Brugerolle and Metenier (1973)